EXHIBIT 8

Louis J Mini/LAKE/PPRD/ABBOTT

03/02/2004 06:29:33 PM GMT

To Charles Schwamlein/LAKE/PPRD/ABBOTT@ABBOTT
cc James Embrescia/LAKE/PPRD/ABBOTT@ABBOTT, John J Kody/LAKE/PPD/ABBOTT@ABBOTT, Steven E Townsend/LAKE/PPRD/ABBOTT@ABBOTT, William N Kormany/LAKE/PPRD/ABBOTT@ABBOTT
bcc
Subject Re: abstract for submission to teratology

Thanks Charles,

I agree that the only thing that I really find of any concern is the last sentence of the abstract discussion, and I agree with your position on that. Perhaps phrasing something like the following may be better;

"When consulting women of childbearing age, risk of teratogenicity should be an important factor in selecting therapy."

Also, I just received the "revised" valproate AED Pregnancy Registry manuscript, and although the authors did not fully incorporate ALL our comments, they did indeed change most of the "major" ones, such as;

--Changing the title from "Valproate Monotherapy is a Potent Teratogen in Humans" to one identical to this abstract -- "Evidence of Increased Birth Defects in the Offspring of Women Exposed to Valproate during Pregnancy: Findings from the AED Pregnancy Registry"
--Removing the word "potent teratogen" throughout the paper
--Removng the conclusion sentence "VPA is a potent teratogen in humans, and its use should be reduced to the minimum, or substituted by another safer, AED". They again changed the sentence to reflect verbiage consistent with this abstract draft, instead stating "alternative therapies should be considered." --

Overall , much better.

So it appears our input did make a difference. Good Job Charles

Lou

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Schwamlein 03/01/2004 04:33 PM

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cc:
Subject: abstract for submission to teratology

Recall that we met regarding a proposed manuscript for valprate from the Antiepileptic Drug Registry. Appended is an abstract from that manuscript which has been prepared for submission to the Teratology Society.

Please review and give me any comments as soon as possible. My only comment concerns the last sentence. In considereing the alternatives to valproate, there is little information since the registry has not yet found any drugs to be safe, as such. It's only that the data regarding phenobarbital and valproate have been analyzable because of numbers.

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Title:	Evidence of Increased Birth Defects in the Offspring of Women Exposed to Valproate during Pregnancy: Findings from the AED Pregnancy Registry
Authors & affiliations:	Rachel M. Alsdorf[1], Diego F. Wyszynski[1], **Maya Nambisan[2], Triptaa Surve[2], Lewis B. Holmes[2,3]**, for the Antiepileptic Drug (AED) Pregnancy Registry[3],[1]Genetics Program, Department of Medicine, Boston University School of Medicine; [2]Genetics and Teratology Unit, Pediatric Service, Massachusetts General Hospital; [3]Department of Pediatrics, Harvard Medical School, Boston, Massachusetts
Abstract: (Your abstract must use Normal style and must fit in this space)	Introduction: Valproic acid is widely used as an effective anticonvulsant, anti-migraine agent, and in the management of bipolar disorders. All of these conditions occur frequently in women of childbearing age. Monotherapy valproic acid (VPA) use during the first trimester of gestation has been associated with an increased risk for spina bifida and other major congenital anomalies in the newborn. However, most studies have been hampered by a small number of exposed pregnancies and a retrospective design. Methods: Data were collected by the Antiepileptic Drug (AED) Pregnancy Registry from pregnant women throughout the U.S. and Canada who were taking an anticonvulsant drug. The prevalence of congenital malformations among offspring of monotherapy VPA exposed women was compared to that among infants of women exposed to all other AEDs ("internal comparison group"), and to that among newborns in the Active Malformations Surveillance Program at Brigham and Women's Hospital ("external comparison group"). Results: Sixteen affected cases were identified among 149 VPA exposed women (proportion: 10.7%, 95% confidence interval [CI]: 6.3-16.9%). The prevalence in the internal comparison group was 2.9% (95% CI: 2.0-4.1%; odds ratio: 4.0, 95% CI: 2.1-7.4; $p < 0.001$). Assuming a 1.62% prevalence in the external comparison group, the relative risk to having an affected offspring for VPA-exposed women was 7.3 (95% CI: 4.4-12.2; $p < 0.001$). Discussion: Maternal exposure to VPA during the first trimester of pregnancy significantly increases teratogenicity in humans. When consulting women of childbearing age, alternate therapies should be considered. **Supported by Abbott, Elan, GlaxoSmithKline, Ortho-McNeil, Novartis, and Pfizer**

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